[redacted]

P-18-0136

Chemical Name: [redacted]

CASRN: [redacted]

ASSIGNMENTS	NAME	DATE
SAT Chair	Doritza Pagan-Rodriguez	04/24/18
HH Hazard Assessor (A)	Keith Salazar	04/24/18
HH Hazard QC Reviewer (A)	Iris Camacho	04/27/18
HH Risk Assessor FOCUS (B)	Keith Salazar	05/03/18
HH Risk QC Reviewer (B)	Sharon Oxendine	05/03/18

Human Health Report Status:		DATE COMPLETED
X	HAZARD DRAFT- Pending Review	
X	HAZARD REVIEWED	04/27/18
x	HAZARD FINAL	04/30/18
x	RISK DRAFT- pending review	05/01/18
x	RISK REVIEWED	
x	RISK-FOCUS FINAL- Uploaded	05/03/18
	POST-FOCUS UPDATE DRAFT	
	POST-FOCUS UPDATE FINAL- Uploaded	

Updated 10/16/18 to reflect no concern for irritation based on submitted PMN data and to reflect that exposure is unlikely as the [redacted] are contained inside cartridges. Updates only made the summary bullets. Edits in red.

[redacted]

1 HUMAN HEALTH SUMMARY

EPA estimated the human health hazard of this chemical substance based on its estimated physical/chemical properties, available PMN data, and by comparing it to structurally analogous chemical substances for which there is information on human health hazard. EPA concludes there is low/moderate concern for human health hazard for the chemical substance.

Based on the hazard determination and available qualitative risk information, EPA concludes that there is risk for the PMN substance. The risk estimates for this chemical are for the intended conditions of use. Other conditions of use and their risks were not evaluated.

1.1 Hazard Summary

- Absorption is expected to be nil through the skin (pchem, solubility, high MW, physical state, ionized state), and poor to nil through the GI tract and lungs (pchem and submitted data).
- Concern for systemic toxicity from repeated exposures to the PMN substance's anion based on moderate acute toxicity observed in submitted analog data.
- Concern for irritation to all exposed tissues (skin, eyes, mucous membranes, GI tract, lungs) for the cation based on data submitted for an analogue. Concern mitigated by submitted negative irritation data on the PMN.

1.2 Risk Summary

1.2.1 Workers

- Although analog data indicates that the new chemical could result in systemic effects, potential risks were not identified for workers via inhalation or dermal exposure because exposure was expected to be negligible.

1.2.2 General Population

- Although analog data indicates that the new chemical could result in systemic effects, potential risks were not identified for the general population via inhalation or oral exposures because exposure was below modeling thresholds.

1.2.3 Consumers

- Risks were not identified for consumers because no uses were identified.

[redacted]

~~1.3 Testing Recommendations:~~ PUI

~~OECD Test Guideline 407 28-day oral toxicity study to clarify the concern for systemic toxicity~~

- Specific target organ toxicity

[redacted]

2 HUMAN HEALTH HAZARD- PART A

2.1 Chemistry Summary

PMN: P-18-0136	Submitter: [redacted]			Manu.	Import
Max. PV (KG): [redacted]		Binding Option Marked:			[redacted]
MW: [redacted]		% < 500		% <1000	CASN[redacted]

PMN Structure	Prop.	Meas.	Est.
[redacted]	MP		
	BP		
	Pres.		at 760 mm Hg
	VP		<0.000001
	S-H2O	2.067	
	log P	1.74	

[redacted]	Analogs: [redacted]
USE: [redacted] All analogs are dyes for [redacted]	other_uses No other uses were found for the PMN material.

2.1 SAT Summary

2.1.1 PMN Health Rating

- 1-2

2.1.2 SAT Key Words

- AQUATOX, IRRITATION, SYSTEMIC

2.1.3 Absorption

- Absorption is expected to be nil through the skin (physical chemistry), and poor to nil through the GI tract and lungs (pchem and submitted data).

[redacted]

2.1.4 SAT Health Summary

- Concern for systemic toxicity from repeated exposures to the LVE substance's anion based on moderate acute toxicity observed in submitted analog data. There is concern for irritation to all exposed tissues (skin, eyes, mucous membranes, GI tract, lungs) for the cation based on data submitted with [redacted].

2.1.5 PMN Data (Study summary, POD)

- Note: EPA determined that the analog submitted data were not appropriate for the LVE's cation.
- LLNA negative (analog)
- OECD TG 404 Acute Dermal (PMN): no irritating or corrosive effects in rabbits
- OECD TG 437 Bovine Corneal Opacity test (PMN): inconclusive; clouding of tissue
- OECD TG 439 In vitro skin irritation in reconstructed human epidermis (PMN): inconclusive; test substance not compatible with test
- OECD TG 474 Mammalian micronucleus test (analog): no significant increase in micronucleated polychromatic erythrocytes. Non clastogenic.
- OECD TG 471(analog) Bacterial reverse mutation test: not mutagenic
- OECD 423(analog) acute oral toxicity: Clinical signs observed included lethargy, hunched posture, labored respiration, piloerection, ptosis, and uncoordinated movements. No abnormalities were found at macroscopic post mortem examination of the animals. According to the test guideline, the LD_{50} cut-off value was considered to be 500 mg/kg-day

[redacted]

2.1.6 Analog Data (analog, structure, study summary, POD)

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(38) ANALOGS:

PMN or CAS No.	Chem. Name	Structure	TSCA Y/N
[redacted]			

- [redacted] (anion)
  - [redacted] (-) Salmonella with and without activation; (-) E. coli with and without activation; (-) ip mouse micronucleus assay (highest dose tested 15 mg/kg because of toxicity to the mice); rat oral LD50 >300 mg/kg <2000 mg/kg; no eye irritation in rabbits; no skin irritation in rabbits; no skin sensitization in mice using the local lymph node assay
- [redacted] (anion)
  - (-) Salmonella with and without activation; (-) E. coli with and without activation; (-) for chromosome aberrations in human lymphocytes with and without activation; rat oral LD0 = 2000 mg/kg; rat dermal LD0 = 2000 mg/kg; no skin irritation in rabbits; corrosive to eyes in rabbits, corneal opacity and vascularization; no skin sensitization in guinea pigs using the Magnusson-Kligman assay; rat 28-d oral NOEL = 150 mg/kg, effects on stomach, appears to be irritation
- [redacted] (analog for cation)

[redacted]

- [redacted]
- From AIM: Negative in Salmonella, E. coli, and mouse micronucleous assay Not a dermal sensitizer in guinea pigs LC50 > 2.57 mg/l in rats; irregular respiration observed. LC50 > 2.58 mg/l in rats (analog data) Irritating to rabbit skin Dermal LD50 > 250 mg/kg in rabbits; no mortality; reversible skin irritation observed. acute dermal toxicity study - Severe toxicity (such as distress) and mortality observed at 1000 and 2000 mg/kg. NOAEL was not determined. acute dermal toxicity/irritation - Mortality and skin necrosis observed at 500 mg/kg. No effects observed at 250 mg/kg. Oral LD50 550 mg/kg in female rats; (1/4 and 3/3 rats died at 550 and 2000 mg/kg, respectively). 5-d oral study - 2/6 female and 1/6 male rats died after treatment with 1000 mg/kg undiluted. Clinical signs (such as burrowing, salivation, ptosis, piloerection, wobbly gait, tremors, twitching, and convolutions) were observed in animals treated with 1000 mg/kg of the diluted test material. 18-d oral No effects were observed in treatment groups, except for transient clinical signs (wobbly gait, passivity, tremors) in the high dose group (1000 mg/kg) during days 1-2 of treatment. 28-d oral- NOAEL = 500 mg/kg based on hyperemia in the glandular portion of the stomach observed in animals from the 1000 mg/kg group. Clinical signs were observed in all treated animals, but were attributed to irritation because the neurological assessment was unremarkable. SAT does not necessarily agree with this conclusion from study authors. Data on [redacted]: Dermal LD50 > 25 mg/kg and < 50 mg/kg; test material was severely irritating and caused tremors prior to death [redacted]. Not a dermal sensitizer in guinea pigs

2.1.7 Other Information (SDS, structural alert or component of interest, basis, etc.)

- NOTE: due to the high water solubility, the PMN is not expected to be a lung surfactant

2.1.8 Exposure Routes of Interest

Route of Interest	
x	Inhalation:
x	Dermal:
x	Ingestion:

2.2 Human Health Category (From US EPA 2010 document)

Chemical Category: Chemical Category Health Concerns: Category Testing Strategy:

2.3 Point of Departure Selected and Basis

2.3.1 POD for Oral exposures for the anion

POD type: NOAEL

[redacted]

POD Value: 150 mg/kg-day

POD Chemical: [redacted]

POD Route: Oral

POD Hazard Endpoint: Stomach/ GI

POD Basis: Lowest POD

POD Benchmark MOE: 100

Reference: [redacted]

2.3.2 POD for Oral exposures for the cation

POD type: NOAEL

POD Value: 500 mg/kg-day

POD Chemical: [redacted]

POD Route: Oral

POD Hazard Endpoint: Stomach/ GI

POD Basis: Lowest POD

POD Benchmark MOE: 100

[redacted]

[redacted]

3 HUMAN HEALTH RISK (PART B)

3.1 USES and EXPOSURES

3.1.1 Uses

- [redacted]

3.1.2 Worker Exposure

3.1.2.1 Inhalation

- negligible (VP < 0.001 torr)

3.1.2.2 Dermal

- Potential Dose Rate: [redacted]

3.1.3 General Population Exposure:

- All predicted environmental releases to air, incineration, and/or landfill are below modeling assessment thresholds

3.1.3.1 Drinking Water

3.1.3.2 Fish

3.1.3.3 Air/Inhalation

3.1.4 Consumer Exposure

- No reasonably anticipated consumer exposures;

3.2 RISK CALCULATIONS

3.2.1 Worker Calculations

	Animal or Human			Human							Benchmark MOE	Endpoint Type
Exposure Route	POD mg/kg-day	POD Exposure Duration Days/Wk	POD Route % Absorp	Exposure mg/day Potential Dose Rate (PDR)	Exposure Duration Days/Wk	Exposure Route % Absorp	Body Weight kg	Exposure mg/kg-day	Structural Alert as % of PMN	Margin of Exposure MOE	100	NOAEL
Inhalation		[redacted]	100%		[redacted]	100%	80	0.0E+00	100%	#DIV/0!	Fold Factor = #DIV/0!	
Dermal	1.5E+02	[redacted]	100%	[redacted]	[redacted]	0%	80	5.5E-01	100%	272727.3	[redacted]	

Risks were not identified for workers, for GI effects via dermal exposure based on quantitative hazard data for an analog (MOE > 270,000 benchmark MOE =100).

[redacted]

3.2.2 General Population Calculations

Risks were not assessed because general population exposures are not expected

3.2.3 Consumer Calculations

Risks were not assessed because consumer exposures are not expected